Available online at www.sciencedirect.com
SCIENCE DIRECT®
Toxicology Letters 137 (2003) 103–110
Toxicology Letters
www.elsevier.com/locate/toxlet

Essentiality and toxicity of selenium and its status in Australia: a review

Ujang Tinggi *

Queensland Health Scientific Services, Centre for Public Health Sciences, 39 Kessels Road, Coopers Plains, Brisbane, Qld. 4108, Australia

Abstract

Selenium (Se) is an essential trace element for animals and humans because of its role in an antioxidant enzyme glutathione peroxidase. This enzyme protects cell membranes from damage caused by the peroxidation of lipids. The paper provides an overview of the effects of Se toxicity and deficiency in humans and animals. It is well established that Se deficiency causes health implications in humans and animals. Se is also very toxic and can cause Se poisoning (selenosis) in humans and animals. In Australia, Se deficiency has caused health problem to livestock; however, the problems were eliminated after the introduction of Se supplementation. Se toxicity has also been reported in some regions of Australia as a result of livestock feeding on Se accumulative plant species. The major source of Se is diet, and in many regions of the world the levels of Se in the soils generally reflect the Se status in human populations. In foods, the bioavailability and toxicity of Se depend on its chemical forms. Generally, organic forms of Se are more bioavailable and less toxic than the inorganic forms (selenites, selenates). The Se status in the Australian population and how this is compared with the rest of the world is also discussed.

Keywords: Selenium; Selenium toxicity; Selenium deficiency; Selenium status

1. Introduction

The early works by veterinary scientists and animal nutritionists have provided important groundwork in Se research in Australia in terms of addressing the effects of selenium (Se) toxicity and deficiency on livestock and agricultural production (Underwood, 1977). The results of this early investigation have led to an introduction of Se supplementation in animal nutrition for improvement of animal health and production in Australia. In the case of human research, interest in Se in Australia came much later, and this was particularly stimulated by reports on the health effects of Se deficiency and toxicity in some parts of China and low Se status in the New Zealand population.

In many countries including Australia, there have been no reports of human disease associated with Se deficiency and toxicity. However, diseases associated with Se deficiency are still a cause of concern in many countries, and in particular in countries of low Se status such as Finland and New Zealand. These two countries have introduced policies to increase Se status in the human

* Tel.: +61-7-3274-9144; fax: +61-7-3274-9186.
E-mail address: ujang_tinggi@health.qld.gov.au (U. Tinggi).

0378-4274/02/$ - see front matter.
PII: S0378-4274(02)00384-3

population, by adding Se fertilisers to agricultural crops in Finland, and the importation of Se-rich foods such as Australian wheat for New Zealander diet (Aro et al., 1995; Thomson and Robinson, 1996). While there is no immediate concern with regard to Se status in the Australian human population, there have been reported cases of low Se status in farm animals (Dreosti, 1986).

In the past two decades there has been much progress in our knowledge and understanding of the biological roles of Se and its importance in human and animal nutrition. This recent interest in Se has been further stimulated by new findings of several selenoproteins in animals. Even though the functional roles of these selenoproteins are not fully understood, there is increasing evidence that these selenoproteins and other Se metabolites are important in immune function and reduced cancer risk. The current knowledge of Se role in health and disease is important in assessing the health risk associated with low Se status in a population.

2. Selenium chemistry

Se was discovered in 1817 by Swedish chemist, Jons Jacob Berzelius, while analysing a red deposit on the wall of lead chambers used in the production of sulphuric acid. Se is classified as a metalloid that lies between sulphur and tellurium in Group VIA and between arsenic and bromine in Period 4 of the periodic table. Se closely resembles sulphur in chemical properties with respect to atomic size, bond energies, ionisation potentials and electron affinities. The major difference between two these elements is that Se exists as reduced quadrivalent form whereas sulphur occurs as oxidised quadrivalent form. In addition, there is also a difference in acid strengths between these two elements. For instance, selenium hydride (H_2Se) is a stronger acid ($pK_a = 3.7$) than sulphur hydride (H_2S, $pK_a = 6.9$). Due to its greater acid strength, Se as selenol compounds (R–SeH) are readily dissociated at physiological pH which are important for their roles in catalytic reaction. Se can also exist in various oxidation states and these allow it to form into several organic Se compounds (dimethylselenide, trimethyselenium) and in amino acids (selenomethionine, selenocysteine) in place of sulphur.

3. Selenium essentiality

Since the discovery of Se in 1957 as an essential trace element in preventing liver necrosis in vitamin E deficient animals, interest in Se research has increased considerably, particularly in the livestock industry (Schwarz and Foltz, 1957). In 1973 Se was identified to be an important component of glutathione peroxidase (GSHPx), which is characterised as a tetrameric protein with four atoms of Se per molecule (Rotruck et al., 1973). This GSHPx assists in intracellular defense mechanisms against oxidative damage by preventing the production of active oxygen species (Ursini and Bindoli, 1987). In the 1980s further selenoproteins were discovered which indicated that Se is not merely restricted to its role in antioxidant activity but also involved in other multiple aspects of mammalian metabolism. More recently, Se has been shown to be an important component of iodothyronine deiodonase, an enzyme which is a selenoprotein, and also as a functional selenoprotein in thioredoxin reductase (Arthur et al., 1993; Gladyshev and Hatfield, 1999). The pathways of Se metabolism in animals is presented in Fig. 1.

Diseases associated with Se deficiency have been a serious problem in farm animals in many parts of the world. For instance, hepatosis dietetica, a liver necrosis can cause death to pigs within hours after the symptoms appeared, and exudative diathesis can cause death to poultry within a few days as result of oedema of body tissues. The most common Se deficiency disease is the white muscle disease, which is a nutritional muscular dystrophy. A high incidence of the white muscle disease in sheep and cattle was reported in New Zealand and western Oregon, USA (Andrews et al., 1968; Wolf et al., 1963). This deficiency disorder occurs particularly in growing animals, and subsequently mainly affects lambs from 1 to 3 months old. The lambs become weak and difficult to feed, and if cardiac implication occurs, the sudden death is often the result. In Australia, the white muscle disease in sheep has been reported in some regions.

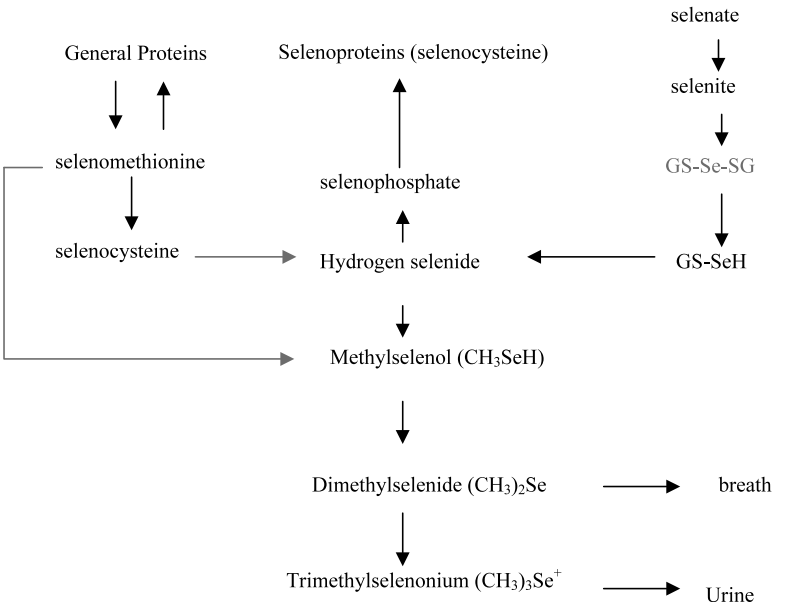

Fig. 1. Metabolism of selenium in animals.

However, there are many factors that could contribute to this disease, and these may include low Se status in fodder such as clover, complications caused by other mineral deficiencies, poor summer nutrition and animal general health status (Peter and Costa, 1992). Even though there were no major outbreaks of Se deficiency diseases in Australian farm animals, there have been reports of subclinical Se deficiencies in some areas that resulted in losses of production (Reilly, 1996). The symptoms of subclinical Se deficiencies are more difficult to detect, but usually these are associated with depressed growth and production, and impaired immune response. Due to the concerns of the effect of these subclinical Se deficiencies on animal production, a number of strategies of Se supplementation were introduced in Australia to increase Se status to these animals. These strategies include: (1) direct application of Se to pastures to increase Se uptake by plants for animal feed; (2) supply of sodium selenite or selenate which are incorporated into salt blocks or licks; (3) direct administration of Se to animals by drenching with Se salt solutions such as sodium selenite; (4) and the use of Se pellets that slowly release Se in animal gut.

The first reported cases of Se deficiency disease in human population occurred in China. The Se-responsive disease known as Keshan's disease is a cardiomyopathy, which mainly affects young children and women of child bearing age has occurred in some areas of China where the soil is low in Se (Chen et al., 1980). The introduction of Se salt as sodium selenite to supplement Se dietary intake to this endemic population has reduced the incidence of these disorders. Another Se-responsive disease, also reported in areas of China, is Kaschin–Beck disease, which is an osteoarthropathy, a generative articular disease caused by oxidative damage to cartilage that leads to deformation of bone structure (Ge and Yang, 1993).

4. Selenium toxicity

Se toxicity in animals was widely recognised in the 1930s in South Dakota, when it was discovered that livestock grazed in area of high Se soil developed the disorders known as 'alkali disease' and 'blind staggers' (Magg and Glen, 1967). The 'alkali disease' is a chronic poisoning of horses and cattle from continuous ingestion of plants contain-

ing over 5 but usually less than 50 mg/kg Se. These low Se accumulating plants are classified as secondary indicator plants. The disease is characterised by dystrophic changes in hooves and rough hair coat. The early observation of Se toxicity could probably be reported by Marco Polo during his travel to some regions of China in 13th century when he described a disease called 'hoof rot' in horses, where area of high Se soil exists. The 'blind staggers' is also a chronic poisoning in animals which often associated with feeding on plant species, classified as primary indicator plants, that can naturally accumulate Se up to 1000 mg/kg. The signs of the disease include weight loss, blindness, ataxia, disorientation and respiratory distress.

These outbreaks of Se poisoning or selenosis are not a major problem for animal producers in most parts of the world. However, in Australia, a similar disorder of 'alkali disease' has been reported in horses which grazed on the shrub, *Morinda reticulata*, which grows specifically in the northern region of Queensland (Knott and McCray, 1959). Subsequent analysis of this plant indicated that it is can accumulate Se in its tissue at high levels. Another Se accumulating plant species, *Neptunia amplexicaulis*, which caused selenosis to farm animals has also been reported in Queensland area (Peterson and Butler, 1967). These Se accumulating plant species were found to contain selenocystathionine, an organic form of Se that is toxic to animals. Selenocystathionine will finally be metabolised and converted to selenomethionine, which is a predominant form of Se compounds in tissues of plants, algae and yeast. Fig. 2 shows the pathways of Se metabolism and the selenomethionine biosynthesis in plants.

Even though the use of Se in industry and agriculture has increased considerably in the past four decades, there have been no reports of major Se environmental toxicity in most parts of the world, except for the deaths and deformities of fish and water birds in Kerterson National Wildlife Refuge in southern California (Ohlendorf et al., 1990). This Wildlife Refuge was established in response to the concern about the loss of much of the wetlands because of expanding agricultural activities. The water for the Wildlife Refuge wetland was supplied through the Kesterson reservoir that consisted of a series of 12 ponds for agricultural water drainage, storage, evaporation and recycling facilities. The deaths and deformities to wildlife in the area were associated with contamination of Se, predominantly as soluble selenates in the water that were as high as 30 μg/l (Fan et al., 1988). High Se levels in tissues of wildlife in the area were also found. However, a health survey of residents and domestic animals living within the area did not show any adverse health effects, despite of heavy Se contamination.

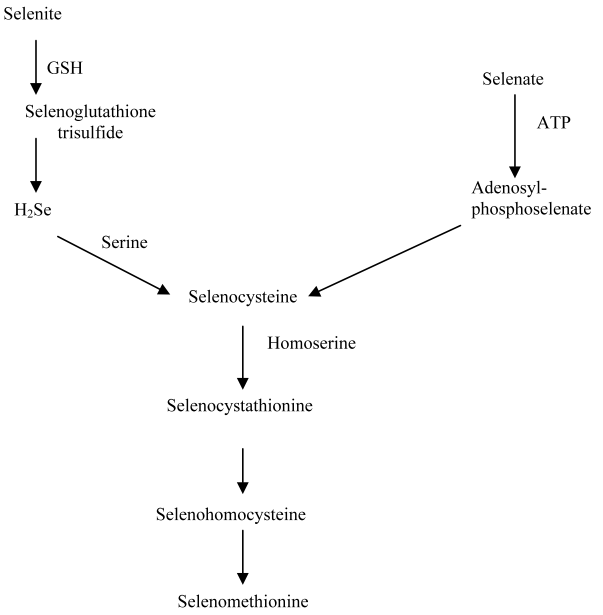

Fig. 2. Selenomethionine biosynthesis in plants.

Environmental toxicity of Se in humans is rare, however, the effects of Se toxicity have been reported to cause hypochromic anaemia and leucopenia, and damaged nails to long-term workers employed in the manufacture of Se rectifiers (Rosenfeld and Beath, 1964). There have been a number of cases of reported acute and subacute Se poisoning in humans as a result of accidental ingestion of selenic acid (30 g/l) and vitamin tablets that contained high levels of Se. An ingestion of Se at high level is reported to cause gastrointestinal disturbances (vomiting, diarrhea), hair and nail changes, and neurologic manifestations including acroparesthesias, weakness, convulsions, and de-

creased cognitive function (Clark et al., 1996; Gasmi et al., 1997).

Even though there has been tremendous research on Se toxicity in animals, the mode of actions of Se at cellular and molecular levels is not yet fully understood. Recently, it has been suggested that Se toxicity may be due to the interaction of selenite with glutathione to form reactive selenotrisulfides to produce toxic superoxide and hydrogen peroxide (Spallohlz, 1994). Until there is further knowledge on the specific effect of Se toxicity in the body tissue, its additional use as dietary supplementation should be approached with caution. In addition, toxicity of Se not only depends on the chemical form and quantity of the element consumed, but also on a variety of other factors that include species, age, physiological state, nutrition and dietary interactions, and the route of administration.

5. Selenium status and intake

The levels of Se and the activities of GSHPx in blood plasma have been widely used as biomarkers for assessing Se status in humans and animals (Neve, 1995). Recently, the levels of selenoprotein P, a Se-rich protein found mainly in blood plasma, have also been shown to be a good indicator for Se status in humans (Persson-Moschos et al., 1995). The activities of GSHPx and Se levels in blood are influenced by diet and food intakes, which are the principal source of Se. The levels of Se in foods tend to reflect the levels of Se in soils. In some regions of China, it has been shown that Se intakes of people from areas of low Se soil are significantly lower than those from areas of high Se soil (Yang, 1985). High Se intakes have also been reported in Venezuela and South Dakota, USA, which reflect the high levels of Se in soils and agricultural produce in the regions (Olson and Palmer, 1984; Bratter et al., 1993). A number of studies have also been carried out in European countries and the levels of Se intakes for these countries are relatively low (Alfthan et al., 1992; Neve, 1991). Table 1 shows the daily intakes of Se from selected countries.

Table 1
Estimated selenium intakes (μg/day) from selected countries

Country	Se (μg/day)	Reference
Belgium	28–61	Robberecht et al., 1994
Canada	98–224	Gissel-Nielsen, 1998
China		
Low Se area (Keshan disease)	2–36	Luo et al., 1985
High Se area (selenosis)	240–6990	Yang et al., 1983
Finland		
Before using Se fertiliser	25	Aro et al., 1995
After using Se fertiliser	67–110	Anttolainen et al., 1996
Greece	110	Bratakos et al., 1990
Hungary	41–90	Alfthan et al., 1992
Japan	104–127	Suzuki et al., 1988
New Zealand	19–80	Robinson and Thomson, 1987
UK		
England	12–43	Barclay et al., 1995
Scotland	30–60	MacPherson et al., 1997 Shortt et al., 1997
USA	60–160	Longnecker et al., 1991
South Dakota	68–444	Swanson et al., 1990
Venezuela	200–350	Combs and Combs, 1986
Mexico	61–73	Valentine et al., 1994

In Australia, there has been a limited study of Se dietary intakes in the population. The importance of human Se dietary research in Australia and the need for dietary data in order to fill the gap in this knowledge has been expressed (Reilly, 1993). Reilly et al. (1990) have undertaken a study of Se dietary intakes in healthy young children and their siblings with phenylketonuria. However, it has been estimated that the levels of Se dietary intakes in Australia could be considered moderate, particularly in comparison to the USA intakes (Reilly, 1992). For the Australian adults, the estimated Se intakes ranged from 57 to 87 μg/day (Farady et al., 1989). The National Health and Medical Research Council (NHMRC, 1991) has established a Recommended Daily Intakes (RDI) for Se in Australia (Table 2). Due to the limited data available for Se dietary survey in Australia, the estimation for the Australian RDI is based on the data from other countries.

Table 2
Australian recommended dietary intakes for selenium (NHMRC, 1991)

Age group	μg/day
Infants	
0–6 months	10
7–12 months	15
Children	
1–3 years	25
4–7 years	30
Adolescents	
8–11 years	50
12–18 years	85
Adults	
19–64 years	
Males	85
Females	70
Pregnancy	+10
Lactation	+15

The major food source of Se in Australia comes from wheat products such as bread and cereals (Tinggi et al., 1992). Australian meat products also contained relatively high levels of Se in comparison to other countries (Tinggi, 1999). Table 3 shows the content of Se in selected Australian foods. A survey of Se contents of Australian cow's milk showed a wide variation with higher levels in summer, and the contribution of milk to Se dietary intakes is considerable, particularly for infants (Tinggi et al., 2001). A study of breast milk consumption by infants in Queensland has also shown that breast milk is a good source of Se dietary intake (Cumming et al., 1992).

Table 3
Selenium levels (mg/kg) in selected Australian foods

Food	Se (mg/kg)
Cereal, cereal products	0.01–0.31
Bread	0.06–0.15
Rice (white)	0.05–0.08
Pasta/spaghetti	0.01–0.10
Meat, meat products	0.06–0.34
Chicken	0.081–0.142
Pork	0.032–0.198
Beef	0.042–0.142
Lamb	0.033–0.260
Milk, dairy products	<0.001–0.11
Cow's milk	6.7–47.6 μg/l
Summer milk	23.8±4.6 μg/l
Autumn milk	20.9±4.4 μg/l
Winter milk	20.7±4.2 μg/l
Spring milk	20.6±4.8 μg/l
Vegetables, fruit	<0.001–0.022

Tinggi et al. (1992), Tinggi (1999), Tinggi et al. (2001).

6. Conclusions

Australia has experienced both Se poisoning and deficiency diseases in domestic and farm animals. The disease, particularly associated with subclinical Se deficiency, has largely been eliminated as a result of intervention programs of introducing Se supplementation to animals. In the case of human population, no associated health problems were encountered in Australia. However, as there is increasing evidence of linking low Se status to cancer risk and immune function, there has also an increased interest in Se supplementation in the population. In Australia there is a restriction on the use of Se as a dietary supplement due to real concern of toxicity and over-zealous misuse of its supplementary intake. There is also a need in Australia to undertake a detailed study of Se status and dietary intake in the general population, and to establish a database that could be used to reassess the adequacy of diets in supplying Se in ever changing dietary habit in the population. The provision of an available database would also be important in dealing with emerging health issues related to Se imbalance and its management in the future.

References

Alfthan, G., Bogye, G., Aro, A., Feher, J., 1992. The human selenium status in Hungary. J. Trace Elem. Electrolytes Health Dis. 6, 233–238.

Andrews, E.D., Hartley, W.J., Grant, A.B., 1968. Selenium-responsive diseases in animals in New Zealand. Vet. J. 16, 3–17.

Anttolainen, M., Valsta, L.M., Alfthan, G., Keemola, P., Salminen, I., Tamminen, M., 1996. Effect of extreme fish consumption on dietary and plasma antioxidant levels and fatty acid composition. Eur. J. Clin. Nutr. 50, 741–746.

Aro, A., Alfthan, G., Varo, P., 1995. Effects of supplementation of fertilizers on human selenium status in Finland. Analyst 120, 841–843.

Arthur, J.R., Nicol, R., Beckett, G.J., 1993. Selenium deficiency, thyroid hormone metabolism, and thyroid hormone deiodinases. Am. J. Clin. Nutr. 57, 236S–239S.

Barclay, M.N.I., MacPherson, A., Dixon, J., 1995. Selenium content of a range of UK foods. J. Food Comp. Anal. 8, 307–318.

Bratakos, M.S., Kanaki, K., Vasiliov-Waite, A., Ioannou, P., 1990. The nutritional selenium status of healthy Greeks. Sci. Total Environ. 96, 161–176.

Bratter, P., de Bratter, N.V.E., Gawlik, D., Oliver, W., Alvarez, N., Jaffe, W., 1993. Selenium in human monitors related to the regional dietary intake levels in Venezuela. J. Trace Elem. Electro. Health Dis. 7, 111–112.

Chen, X., Yang, G., Chen, J., Chen, X., Wen, Z., Ge, K., 1980. Studies on the relations of selenium to Keshan disease. Biol. Trace Elem. Res. 2, 91–104.

Clark, R.F., Strukle, E., Williams, S.R., Manoguerra, A.S., 1996. Selenium poisoning from a nutritional supplement. J. Am. Med. Assoc. 275, 1087–1088.

Combs, G.F., Combs, S.B., 1986. The Role of Selenium in Nutrition. Academic Press, New York, NY, pp. 127–177.

Cumming, F.J., Fardy, J.J., Woodward, D.R., 1992. Selenium and human lactation in Australia: milk and blood selenium levels in lactating women, and selenium intakes of their breast-fed infants. Acta Paediatr. 81, 292–295.

Dreosti, I.E., 1986. Selenium. J. Food Nutr. 43, 61–78.

Fan, A.M., Book, S.A., Neutra, R.R., Epstein, D.M., 1988. Selenium and human heatlh implications in California's San Joaquin Valley. J. Toxicol. Environ. Health 23, 539–559.

Farady, J.J., McOrist, G.D., Farrar, Y.J., 1989. The determination of selenium in the Australian diet using neutron activation analysis. J. Radioanal. Nucl. Chem. A 133, 391–396.

Gasmi, A., Garnier, R., Galliot-Guilley, M., Gaudillat, C., Quartenoud, B., Buisine, A., Djebbar, D., 1997. Acute selenium poisoning. Vet. Hum. Toxicol. 39, 304–308.

Ge, K., Yang, G., 1993. The epidemiology of selenium deficiency in the etiological study of endemic diseases in China. Am. J. Clin. Nutr. Suppl. 57, 259S–263S.

Gissel-Nielsen, G., 1998. Effects of selenium supplementation of field crops. In: Frankenberger, W.T., Jr, Engberg, R.A. (Eds.), Environmental Chemistry of Selenium. Marcel Dekker, New York, pp. 99–112.

Gladyshev, V.N., Hatfield, D.L., 1999. Selenocysteine-containing proteins in mammals. J. Biochem. Sci. 6, 151–160.

Knott, S.G., McCray, C.W.R., 1959. Two naturally occurring outbreaks of selenosis in Queensland. Aust. Vet. J. 35, 161–165.

Longnecker, M.P., Taylor, P.R., Levander, O.A., Howe, S.M., Veillon, C., McAdam, P.A., Patterson, K.Y., Holden, J.M., Stampfer, M.J., Morris, J.S., Willett, W.C., 1991. Selenium in diet, blood, and toenails in relation to human health in a seleniferous area. Am. J. Clin. Nutr. 53, 1288–1294.

Luo, X., Wei, H., Yang, C., Xing, J., Qiao, C., Feng, Y., Liu, S., Liu, Z., Wu, Q., Liu, Y., Stoecker, B.J., Spallholz, J.E., Yang, S.P., 1985. Selenium intake and metabolic balance of 10 men from a low selenium area of China. Am. J. Clin. Nutr. 42, 31–37.

MacPherson, A., Barclay, M.N.I., Scott, R., Yates, R.W.S., 1997. Loss of Canadian wheat imports lowers selenium intake and status of the Scottish population. In: Fischer, P.W.F., L'Abbe, M.R., Cockell, K.A., Gibson, R.S. (Eds.), Trace Elements in Man and Animals-9. NRC Research Press, Ottawa, pp. 203–205.

Magg, D.D., Glen, M.W., 1967. Toxicity of selenium: farm animals. In: Muth, O.H., Oldfield, J.E., Heswig, P.H. (Eds.), Selenium in Biomedicine. Conn. AVI, Westport, pp. 127–140.

National Health and Medical Research Council (NHMRC), 1991. Recommended Dietary Intakes for Use in Australia. Australian Government Publishing Service, Canberra, pp. 25–26.

Neve, J., 1991. Methods in determination of selenium states. J. Trace Elem. Electrolytes Health Dis. 5, 1–17.

Neve, J., 1995. Human selenium supplementation as assessed by changes in blood selenium concentration and glutathione peroxidase activity. J. Trace Elem. Med. Biol. 9, 65–73.

Ohlendorf, H.M., Hothem, R.L., Bunck, C.M., Marois, K.C., 1990. Bioaccumulation of selenium in birds at Kesterson Reservoir. California Arch. Environ. Toxic. Contam. 19, 495–507.

Olson, O.E., Palmer, I.S., 1984. Selenium in foods purchased or produced in South Dakota. J. Food Sci. 49, 446–452.

Persson-Moschos, M., Huang, W., Srikumar, T.S., Akesson, B., 1995. Selenoprotein P in plasma as a biochemical marker of selenium status. Analyst 120, 833–836.

Peter, D.W., Costa, N.D., 1992. Selenium in animal production in Australia. Proc. Nutr. Soc. Aust. 17, 99–108.

Peterson, P.J., Butler, G.W., 1967. Significance of selenocystathionine in an Australian selenium-accumulating plant *Neptunia amplexicaulis*. Nature 213, 599–600.

Reilly, C., 1992. Selenium in Australian health and disease. Proc. Nutr. Soc. Aust. 17, 109–114.

Reilly, C., 1993. Selenium in health and disease: a review. Aust. J. Nutr. Diet 50, 136–144.

Reilly, C., 1996. Selenium in Food and Heatlh. Blackie Academic & Professional, London, p. 338.

Reilly, C., Barrett, J.E., Patterson, C.M., Tinggi, U., Latham, S.L., Marrinan, A., 1990. Trace element nutrition status and dietary intake of children with phenylketonuria. Am. J. Clin. Nutr. 52, 159–165.

Robberecht, H.J., Hendrix, P., van Cauwenbergh, R., Deelstra, H.A., 1994. Actual daily dietary intake of selenium in Belgium using duplicate portion sampling. Z. Lebensm. Unters. Forsch. 199, 251–254.

Robinson, M.F., Thomson, C.D., 1987. Status of the food supply and residents of New Zealand. In: Combs, G.F., Jr, Spallholz, J.E., Levander, O.A., Oldfield, J.E. (Eds.), Selenium in Biology and Medicine. Conn., AVI, Westport, pp. 631–644.

Rosenfeld, I., Beath, O.A., 1964. Selenium, Geobotany, Biochemistry, Toxicity, and Nutrition. Academic Press, New York, p. 294.

Rotruck, J.T., Pope, A.L., Ganther, H.E., Swanson, A.B., Hafeman, D.G., Hoekstra, W.G., 1973. Selenium: biochemical role as a component of glutathione peroxidase. Science 179, 588–590.

Schwarz, K., Foltz, C.M., 1957. Selenium as an integral part of factor 3 against dietary necrotic liver degeneration. J. Am. Chem. Soc. 79, 3292–3293.

Shortt, C.T., Duthie, G.C., Robertson, J.D., Morrice, P.C., Nicol, F., Arthur, J.R., 1997. Selenium status of a group of Scottish adults. Eur. J. Clin. Nutr. 51, 400–404.

Spallohlz, J.E., 1994. On the nature of selenium toxicity and carcinostatic activity. Free Radic. Biol. Med. 17, 45–64.

Suzuki, T., Imai, H., Kobatashi, K., 1988. Dietary intake of selenium in Japanese: an estimation by analysed and reported values in foodstuffs and cooked dishes. J. Jpn. Soc. Nutr. Food Sci. 41, 91–102.

Swanson, C.A., Longnecker, M.P., Veillon, C., Howve, S.M., Levander, O.A., Taylor, P.R., McAdam, P.A., Brown, C., Stampfer, M.J., Wilet, W.C., 1990. Selenium intake, age, gender and smoking in relation to indices of selenium status of adults residing in a seleniferous area. Am. J. Clin. Nutr. 52, 852–862.

Thomson, C.D., Robinson, M.F., 1996. The changing selenium status of New Zealand residents. Eur. J. Clin. Nutr. 50, 107–114.

Tinggi, U., 1999. Determination of selenium in meat products by hydride generation atomic absorption spectrophotometry. J. AOAC 82, 364–367.

Tinggi, U., Reilly, C., Patterson, C., 1992. Determination of selenium in foodstuffs using spectrofluormetry and hydride generation atomic absorption spectrometry. J. Food Comp. Anal. 5, 269–280.

Tinggi, U., Patterson, C., Reilly, C., 2001. Selenium levels in cow's milk from different regions of Australia. Inter. J. Food Sci. Nutr. 52, 43–51.

Underwood, E.J., 1977. Trace Elements in Human and Animal Nutrition, fourth ed.. Academic Press, New York, pp. 302–341.

Ursini, F., Bindoli, A., 1987. The role of selenium peroxidases in the protection against oxidative damage of membranes. Chem. Phys. Lipids 44, 255–276.

Valentine, J.L., Cebrian, M.E., Garcia-Vargos, G.G., Faraji, B., Kuo, J., Gibb, H.J., Lachenbruch, P.A., 1994. Daily selenium intake estimates for residents of arsenic-endemic areas. Environ. Res. 64, 1–9.

Wolf, E., Kollonitsch, V., Kline, C.H., 1963. A survey of selenium treatment in livestock production. Agric. Food Chem. 11, 355–360.

Yang, G.Q., 1985. Keshan Disease: an endemic selenium related deficiency disease. In: Chandra, R.K. (Ed.), Trace Elements in Nutrition of Children. Raven Press, New York, pp. 273–288.

Yang, G., Wang, S., Zhou, R., Sun, S., 1983. Endemic selenium intoxication of humans in China. Am. J. Clin. Nutr. 37, 872–881.